

Supporting Information
for
Agricultural Insecticides Threaten Surface Waters at the Global Scale

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SI Methods

Literature search and selection criteria

We performed an exhaustive literature search (1), using multiple search criteria, e.g., “(insecticide* or pesticide* or organophos* or organochlori* or carbamat* or pyrethroid* or neonicotinoid*) and (stream* or ditch* or lake* or pond* or river* or creek)”, of online databases, including ISI Web of Science (1945–June 2012), Biological Abstracts (1926–June 2012), BIOSIS Previews (1926–June 2012), CAB Abstracts (1910–June 2012), CAB Reviews (2003–June 2012), Food Science and Technology Abstracts (1969–June 2012), and Zoological Records (1864–June 2012). To overcome a database coverage bias (2), that is, the systematic exclusion of articles written in languages other than English, we considered articles written in the following eight languages in our literature research: Chinese, English, French, German, Japanese, Russian, Spanish, and Portuguese.

A total of 203,431 database entries resulting from 60 search queries were evaluated in the first step, which was based on the article titles. In the second step, approximately 20,000 articles were checked in greater detail based on the abstract contents, keywords, and, if considered potentially relevant, the main text. Additional studies were identified by footnote chasing (3), i.e., consulting the reference lists of empirical and review papers. This literature search was conducted between June 2006 and June 2012.

For each study considered, the measured insecticide concentration (MIC) reported therein had to meet a series of criteria to be included in the meta-analysis. Specifically, the MIC had to (i) result from agricultural nonpoint sources, which excluded the often extremely high concentrations related to point sources, urban, industrial, and public health activities (e.g., mosquito control, Tse-Tse fly control), aquaculture, atmospheric deposition (long-range transport), forest application, sheep dipping, golf course applications, accidental spills, intentional water contamination (e.g., fishing, waste dumping), and in-crop use (rice fields, cranberry bogs, etc.); (ii) originate from perennial freshwater or estuarine surface water bodies (concentrations measured in edge-of-field runoff or ephemeral channels were excluded); (iii) be above the limit of quantification (LOQ, i.e., those concentrations actually detected and quantified) applicable to the respective study to avoid a bias due to artificially high numbers of data points without quantifiable insecticide levels typical for insecticide surface water monitoring (*SI Discussion*) (4); and (iv) be written in one of the languages specified above.

This literature search procedure resulted in the identification of 838 peer-reviewed

publications containing insecticide exposure concentrations, which were included in the present meta-analysis. The meta-analysis is based on peer-reviewed studies to ensure a certain level of data quality, which cannot be claimed to an equal extent for non-peer-reviewed sources, e.g., proceedings or governmental reports (5).

To serve as a quality-control measure for the entire literature search procedure described above, a further independent literature review was performed externally by the scientific literature search service of the “FIZ Karlsruhe” research institution (see http://www.fiz-karlsruhe.de/search_service.html?&L=1). FIZ Karlsruhe performed several search queries in the STN databases AQUALINE (1960–July 2012) and AQUASCI (1978–July 2012) (see <http://www.stn-international.de/index.php?id=123>). In total, 885 bibliographic references, including keywords and abstracts, were provided and analyzed as described above. This independent literature search did not identify any additional relevant articles that had not been identified already in our own literature search.

Each data point consisted of the insecticide’s name, its concentration in water ($\mu\text{g/L}$), sediment or suspended particles ($\mu\text{g/kg}$), the sampling location (including a distinction between a freshwater and an estuarine surface water location), the catchment size, the sampling interval, the sampling date, the LOQ, a classification concerning the certainty that it resulted from an agricultural nonpoint source entry, and the quantity of additional pesticides present in the specific sample. We acknowledge that in very few cases sediment and water samples were taken concurrently at a specific sampling location, which in our analysis, however, constitutes exposure data for different compartments of the aquatic systems under investigation. In cases in which more than one concentration of the same compound resulting from the same insecticide entry event was identified in a certain compartment (e.g., insecticide surface water exposure caused by rainfall-induced runoff or spray drift events sampled with high temporal resolution), we used only one data point (the peak value) to include this event. This step was taken to avoid replicate values that were not independent of one another because such an overlap would have resulted in an overestimation of the total number of independent exposure events. Moreover, we ensured that the equivalent values reported in a number of studies were included only once in the meta-analysis.

We considered endosulfan in our analysis because it is among the only organochlorine insecticides still in agricultural use in many countries (6). Furthermore, we considered a total of six organophosphate insecticides and carbofuran as a carbamate insecticide, which are important insecticides in terms of application rates (7). Finally, all pyrethroid esters (8) and neonicotinoid insecticides were considered, which is justified by the fact that the use of these

two classes of insecticides has increased greatly in recent years to fill the market gaps created by regulatory restrictions on other types of insecticides (9, 10). The concentrations of 16 pyrethroid compounds and four neonicotinoid insecticides measured in agriculturally influenced surface waters were identified and incorporated in the meta-analysis (Table S1).

Regulatory threshold levels for water (RTL_{SW}) and sediment (RTL_{SED})

The insecticide concentrations in water or sediment identified in our meta-analysis were compared with their respective threshold levels. The “regulatory threshold level” (RTL) was used to evaluate the water-phase (RTL_{SW}) and sediment (RTL_{SED}) insecticide concentrations, defining the ecotoxicity endpoint, which allowed for transient adverse ecological effects but was assumed to be ecologically acceptable within the official regulatory insecticide registration procedures (*SI Discussion*).

The RTL_{SW} for North American countries (the US and Canada) were generally derived from the US EPA insecticide registration procedure, whereas the RTL_{SW} applied to European Union member states originated from the European insecticide risk assessment. Both procedures are described in more detail below. The RTL_{SW} used for the evaluation of insecticide concentrations measured in countries outside the US, Canada, or the EU were obtained by calculating the average values of the RTL_{SW} officially used in the US and European risk assessments. These two geographic entities were considered to have rather strict and science-based regulatory procedures for pesticides that could be used for the evaluation of insecticide exposure worldwide. Generally, the concentration of each insecticide was compared with its respective RTL, regardless of how many compounds were measured in a given sample, and the aggregated exceedance frequencies for all studies considered here were computed across multiple sites.

The RTL_{SW} (Table S1) applied to concentrations measured in the US and Canada were derived from the most recent publically available US EPA Office of Pesticide Programs risk assessments for the specific insecticides, e.g., the US EPA’s pesticide Reregistration Eligibility Decision (RED) documents (11), which summarize the acute and chronic toxicity endpoints used in ecological risk assessment for aquatic organisms. In the US acute risk assessments, an estimated environmental concentration is divided by the lowest acute toxicity endpoint (EC₅₀ or LC₅₀) for freshwater and estuarine invertebrates or fish to obtain a risk quotient (RQ). This RQ is then compared with a level of concern (LOC), as defined by the EPA, which is 0.5 for acute aquatic risk. In cases in which the RQ exceeds the LOC, risks exist and appropriate risk mitigation measures must be applied or else no registration will be

granted (for details, see ref. 12). Within the EPA ecological risk assessment, the RTL_{SW} (as used herein) is calculated by multiplying the lowest relevant acute toxicity endpoint by the LOC of 0.5. Apart from insecticide concentrations measured in the EU (see below), we compared concentrations measured in freshwater systems to freshwater RTL_{SW} and those measured in estuarine surface waters to estuarine RTL_{SW} (Table S1). As no US EPA risk assessment documents were available for fenvalerate, the same EPA risk assessment procedure described above was applied using the most sensitive freshwater or estuarine toxicity endpoint, which is provided by core and supplemental studies in the OPP Pesticide Ecotoxicity Database (13). This database contains the currently known ecotoxicity endpoints for registered pesticides used in the US. The toxicity data included in the database are compiled from actual studies reviewed by the EPA in conjunction with pesticide registration or reregistration procedures and have been deemed acceptable for use in ecological risk assessment processes.

In the EU's pesticide risk assessment procedure, the relevant toxicity endpoint is divided by the predicted environmental concentration, resulting in a toxicity exposure ratio (TER). The TER is then compared with trigger values of 100 for the lowest acute toxicity data of the standard freshwater test species or 1 to 10 for the NOEC, NOEAEC, or EAC from a chronic laboratory or higher-tier aquatic micro- or mesocosm study (14, 15). A risk is indicated if the TER is below the relevant trigger value.

For the RTL_{SW} (Table S1) applied to concentrations measured in EU member states, official European pesticide registration documents (16, 17) were evaluated concerning the relevant ecotoxicity endpoints considered within the aquatic risk assessment context. If no documents were available for a certain insecticide at the EU level, the relevant toxicity endpoints and associated trigger values used by the German Federal Office of Consumer Protection and Food Safety (BVL) were used (18). For endosulfan, fenprothrin, fenvalerate, and permethrin, no Europe-wide ecological risk assessment endpoints were available, and the relevant German ecotoxicological effect concentrations and safety factors were applied as European RTL_{SW} . Generally, estuarine or marine organisms are not assessed within the official European pesticide environmental risk assessment so that freshwater RTL_{SW} were applied to all insecticide concentrations measured in the EU irrespective of the type of surface water (Table S1).

In addition to the RTL_{SW} described above, we also evaluated MIC_{SW} using environmental quality standards (EQS). The EQS values (taken from refs. 19-21) were available for 18 insecticide compounds with a corresponding total number of 7,821 MIC_{SW} .

RTL_{SED} are not determined by default for all insecticide compounds within the official US or EU insecticide risk assessment procedures. RTL_{SED} were available from official regulatory risk assessment documents for the following six insecticide compounds: carbofuran, bifenthrin, cypermethrin, cypermethrin-alpha, lambda-cyhalothrin, and tefluthrin (Table S1). The RTL_{SED} derivation is comparable to that described above for RTL_{SW}, with an LOC of 0.5 (in the US EPA risk assessment procedure) and trigger values of 10 (in the EU risk assessment procedure). The insecticide exposure levels detected in sediments or suspended particles for which no sediment RTL_{SED} were available were evaluated by applying maximum permissible concentrations (MPC), as compiled in ref. 19 (Table S1). MPCs (referred to as RTL_{SED} in the main text and the *SI Appendix*) determine the insecticide concentrations in the aquatic environment above which the risk of adverse effects is considered unacceptable provided that the entire aquatic community is taken into account (19). If no MPC was available from ref. 19, we adopted the modified EPA method for aquatic ecosystems, according to which fixed assessment factors were applied to convert acute toxicity data into MPC values for sediment or suspended particles (19, 22). The ecotoxicological endpoints used to apply the modified EPA method originated from the published scientific literature (Table S1). RTL_{SED} were generally applied to all insecticide concentrations in sediments, regardless of their geographic origin.

Further details and corresponding references regarding the RTL derivation of each insecticide considered within this meta-analysis are specified in Table S1.

Insecticide classes

The observed exceedances of RTL_{SW} using aqueous-phase exposure data were compared based on a classification of compounds into three generations of insecticide classes (organochlorines, organophosphates and carbamates, and pyrethroids) included in our meta-analysis. We denote the insecticide class “organophosphates and carbamates” as “organophosphates” in the main text and in the *SI Appendix*. The insecticide generations are defined as classes of insecticides that have been on the market for different periods of time (23) and as insecticide classes that differ with regard to their ecotoxicological mode of action (Table S5) (8). We combined organophosphate and carbamate insecticides into one class because they have been on the market for almost the same amount of time and exhibit the same mode of action (Table S5). For the neonicotinoid insecticide class, only 131 surface water concentrations were available in the peer-reviewed literature. Due to the very small number of cases available, which was further reduced to 72 concentrations available for linear

model analyses (see below), this insecticide class was excluded from all statistical analyses of RTL_{SW} exceedance comparisons for the different insecticide generations.

Classification of countries according to their environmental regulatory quality

To evaluate the influence of the country-specific regulatory standards on global surface water insecticide exposure, we analyzed the data collected for our meta-analysis with regard to differences in observed RTL_{SW} exceedances across countries. We distinguished between countries with well-developed risk assessment and management procedures (referred to here as High Environmental Regulatory Quality or HERQ countries) and those with less well-developed risk assessment procedures and environmental regulatory regimes (Low Environmental Regulatory Quality or LERQ countries) (Table S10). The classification procedure was based on the following three environmental regulatory quality indicators: (i) the “Environmental Regulatory Regime Index“ (ERRI) score (24), which is based on, among other factors, the stringency of environmental standards and environmental regulatory structure and enforcement; (ii) the countries’ regulatory quality percentile rank as one of the World Bank’s global governance indicators (25); and (iii) the World Bank’s main criterion for classifying economies, namely, the gross national income (GNI) per capita (26). According to ref. 24, high levels of per capita income and economic development show a significant correlation with high environmental regulatory quality.

A country’s environmental regulatory quality was categorized as high if (i) the ERRI score of the particular country exceeded one (24) or if (ii) the ERRI score of a particular country was positive or not specified and a country’s regulatory quality rank fell in the upper 25th percentile worldwide (25) and that particular country was classified as a high-income economy with a GNI per capita of \$12,476 or more (26). All other countries were classified as LERQ countries (Table S10).

Statistical analyses: linear model

A linear model analysis was conducted with the logarithm of the aqueous phase measured insecticide concentration to RTL_{SW} ratio as the dependent variable. To determine the effects of the countries’ environmental regulatory quality (Table S10) and the three insecticide classes (Table S5) on the dependent variable, the following independent variables were entered in the analysis using a complete-case approach (27): log sampling interval, log catchment size, sampling date, and the dummy-coded categorical variables for country regulatory classification (HERQ countries [“0”] vs. LERQ countries [“1”]) and insecticide

substance classes (organochlorines ["0"], organophosphates and carbamates ["1"], and pyrethroids ["2"]). The insecticide substance class neonicotinoid was excluded in all linear model analyses due to the low number of concentrations available for complete-case analyses ($n = 72$). The variable sampling interval and catchment size were log-transformed due to the wide spread of the values (minimum/maximum observations $> 1,000$) and a very left-skewed distribution (checked visually).

In the linear model building, all independent variables and interactions were added in sequential steps; that is, first, a main effects model was specified, followed by models containing relevant two-way and three-way interactions (Table S6). We employed automated model building to identify the independent variables and respective interactions with the highest explanatory power for the response variable, namely, the logarithmic insecticide concentration to RTL_{SW} ratio. The automated model building started with the null model (no explanatory variable included) and used backward- and forward-entering variables, with the Bayesian Information Criterion (BIC) used as the goodness-of-fit measure, to identify the best-fit linear models. In addition, manual model building based on expert judgment was performed using the t-test to test the significance of individual predictors and interaction terms and the partial F-test to test for significant differences during model simplification. However, the automated model building and manual model building processes resulted in identical best-fit models. Post hoc probing of interactions was performed by testing simple slopes between groups of the different categorical independent variables (Table S12) and differences between regression lines at specific predicted values of the outcome variable using a modified Johnson–Neyman technique (28) (Table S13).

The models were checked for heteroscedasticity, normal distribution of the residuals, and the influence of single observations (the latter using residual leverage plots and Cook's distance). All computations were performed with the open-source software R (version 2.15.2 for Mac OS X 10.6.8).

SI Discussion

Environmental risk assessment procedure and insecticide field concentrations

The regulatory risk assessment procedure for pesticides requires aquatic exposure data that must be predicted using exposure models because the compounds under assessment are usually not yet on the market (15, 29). These exposure predictions are conducted using realistic worst-case assumptions regarding the variables that determine the pesticide concentration in the non-target environment. In parallel, effect data are derived from laboratory and semi-field model ecosystem experiments (micro- or mesocosms) using various organisms. In the case of aquatic risk assessment predictions for surface waters, effect data are generated for different aquatic organisms. To address uncertainties in the effect assessment, safety factors are often used, i.e., the lowest relevant observed toxicity value from a given ecotoxicological test is divided by a factor between 1 and 100 to derive concentrations that are assumed to be ecologically acceptable (here referred to as regulatory threshold levels, RTL). Comparisons of predicted exposure data and measured effect data, including safety factors (RTL), then indicate either an acceptable environmental risk or the need for specific risk mitigation measures (e.g., no-spray field margins close to surface waters) that become part of the registration procedure as legally binding label amendments for the farmer (30, 31). The pesticide risk assessment procedure, which lasts several years and costs approximately US\$ 25 million per pesticide compound (32), should ensure that pesticide field concentrations do not exceed the RTL, and registration is granted only if these requirements are met. In essence, RTLs denote the maximum threshold concentrations on whose basis individual pesticides are officially approved by regulatory authorities for usage in agriculture, after considering all aspects of exposure predictions, effect assessment, uncertainty, risk management obligations and cost-benefit evaluations. For insecticides in particular, the procedure for determining RTLs often accepts clear but transient effects on aquatic organisms, e.g., RTLs based on so-called “no observed ecologically adverse effect concentrations” derived from mesocosm studies (15), which, however, are assumed to be ecologically acceptable. Consequently, once the insecticide is registered and in use, real exposure levels in the field must ultimately not exceed the RTL to exclude ecologically unacceptable effects, biodiversity losses, and threats to aquatic ecosystems’ structures and functions (33, 34) (Fig. 2A, main text). The comparison of insecticide concentrations measured in agriculturally influenced surface waters to RTLs makes it possible therefore to assess the risks whether and to what extent insecticides potentially cause adverse

environmental effects, which must be avoided according to the regulatory legislation (14, 35).

Comparison with other large-scale studies on insecticide surface water exposure

Agricultural land use and associated insecticide use affect large areas worldwide (36). Despite this fact, few large-scale (e.g., continental) studies consider the insecticide exposure of aquatic ecosystems. For example, the US Geological Survey (USGS; findings summarized in ref. 37) summarized pesticide surface water exposure for 83 agricultural streams across the US and reported that 57% of these 83 stream sites investigated exceeded the regulatory threshold or equivalent water-quality benchmark one or more times during 1992-2001; most of these exceedances involved insecticides exceeding the acute exposure thresholds (37). However, there are several differences between this governmental investigation of insecticide surface water exposure and the meta-analysis presented here: (i) the USGS evaluation encompassed only 10 years (1992-2001); thus, recent insecticide exposure data were not available; (ii) modern, recently increasingly used insecticide classes, such as pyrethroids (with the sole exception of cis-permethrin) and neonicotinoids were not considered, and insecticide exposure in bed sediments was evaluated only for organochlorine insecticides; (iii) the USGS analyzed insecticide exposure data collected at 83 agricultural stream sites; in comparison, our meta-analysis covered more than 2,500 different surface water sites (including streams, rivers, lakes, ponds, estuaries, etc.). However, although the results of our meta-analysis generally support the findings of the USGS monitoring program (i.e., the MICs in surface waters exceed regulatory thresholds, even in highly regulated countries such as the US), they differ in terms of the detected exceedance frequencies per site. In detail, our meta-analysis indicates that although the majority of sites were sampled only once, 68.5% ($n > 1,750$) of these sites were exposed to MICs exceeding their RTL; in contrast, one or more threshold exceedance was reported at only 57% of the 83 agricultural stream sites investigated by the USGS, though each of them had been surveyed several times within a 10-year period (37).

In a narrative review, one publication (38) compiled the surface water concentrations of 38 insecticide compounds, as reported in peer-reviewed literature published between 1982 and 2004, for 15 countries worldwide. However, this study lacked a quantitative data analysis, listed only the minimum and maximum field concentrations ($n = 343$) reported in each field study, and qualitatively compared the maxima ($n = 23$ concentrations) of only a few selected insecticide compounds to various water quality guidelines. By evaluating EU governmental monitoring data on a wide variety of different organic chemicals, ref. 39 recently showed that these compounds threaten the integrity of freshwater ecosystems across the EU. However,

only the maximum and mean concentrations were available for risk evaluation by comparison with acute and chronic standard toxicity data. A recent publication (40) synthesized neonicotinoid surface water concentrations from 29 studies. Although global in scale, this review solely focused on neonicotinoids and reported aquatic exposure data for nine countries only. Finally, ref. 41 compared 122 insecticide field concentrations obtained from 22 scientific field studies to the predicted environmental concentrations (PECs) derived from European pesticide registration documents and disclosed potential deficiencies of the European regulatory exposure assessment. However, in addition to the fact that this publication compared MICs with PECs rather than RTLs, the underlying dataset was substantially smaller than those data presented here and was restricted in geographic scope: only six countries were considered.

We are not aware of further large-scale (e.g., continental) studies or reports targeting agricultural insecticide surface water exposure; thus, we conclude that no comprehensive quantitative global synthesis of insecticide surface water exposure exists that is comparable to the meta-analysis presented here.

Evaluation of insecticide monitoring data

In evaluating pesticide surface water monitoring data, the fact that temporal exposure profiles vary greatly among the various groups of pesticides needs to be considered. Insecticide exposure of surface waters is characterized by infrequent (i.e., 4–6 exposure events per year) and short-term (i.e., a few hours) insecticide concentration peaks (4). Thus, levels exceeding the LOQ in most cases occur only for very short periods (i.e., less than 1% of the year) (4, 42), which holds true for compounds belonging to different insecticide classes (4). It follows that for more than 99% of the time, it is neither feasible nor valid to test the hypothesis that MICs do not exceed their respective RTLs because none of the data that are needed to verify or falsify this hypothesis can be generated. Given this fact, the occurrence of a quantifiable insecticide concentration (i.e., an insecticide concentration > LOQ) is essential as an indicator of whether an insecticide entry event into a surface water body has occurred; these data can be used to test the hypothesis that the insecticide concentration in the field does not exceed the respective RTL. However, it is important to note that aquatic organisms in agricultural surface waters are repeatedly exposed to multiple other pesticides (i.e., herbicides and fungicides) during extended periods of the pesticide application season (43).

Therefore, the data to examine whether the registration procedure is sufficiently conservative and whether insecticide surface water concentrations comply with regulatory risk assessment

outcomes can only consist of cases of samples with insecticide concentrations $> \text{LOQ}$. The sheer number of cases ($n = 11,300$) with MICs $> \text{LOQ}$ available for hypothesis testing within our meta-analysis confirms that MICs largely exceed the RTL at the global scale, i.e., that the cornerstone of regulatory insecticide environmental risk assessment and management is jeopardized by actual field conditions worldwide. Within this context, ref. 4 demonstrated that the use of frequency-based exposure data evaluations involving all insecticide monitoring results (including those below the LOQ), which focus on the probability of threshold level exceedances (e.g., ref. 44) are inappropriate and misleading for compounds with transient exposure patterns, such as insecticides. Ref. 4 also demonstrated that insecticide monitoring datasets must be evaluated using a relevance-driven risk assessment approach; that is, only concentrations $> \text{LOQ}$ are relevant for insecticide exposure assessment.

However, to provide information on the frequency of occurrence of quantifiable insecticide concentrations in the field (these data are often not or only insufficiently provided by the scientific studies included in our meta-analysis) and thereby show the characteristics underlying specific insecticide exposure patterns using field data, we retrieved and analyzed information on the frequencies and numbers of insecticide concentrations $> \text{LOQ}$ obtained from 11 detailed scientific field studies on insecticide surface water exposure (see ref. 4, which provided this information, for details). The evaluation of these monitoring data showed that only 2.6% of the 10,676 field samples collected in these 11 studies contained quantifiable insecticide concentrations. These results are almost identical to the evaluation of large US governmental monitoring datasets derived from the United States Geological Survey (<http://waterdata.usgs.gov/nwis>) and the US Environmental Protection Agency (<http://www.epa.gov/storet/>), which showed that insecticide concentrations were quantifiable (i.e., MIC $> \text{LOQ}$) in only 2.8% of the 3,749,848 insecticide surface water measurements recorded at 14,134 sites across the entire US.

Extrapolating the percentages of samples with quantifiable insecticide concentrations derived from the 11 scientific monitoring studies (i.e., 2.6%) to the data examined in our meta-analysis, the 11,300 MICs $> \text{LOQ}$ analyzed here refer to a population of $n = 434,615$ theoretically analyzed samples in the 838 studies considered. However, for the vast majority of samples ($n = 423,315$; 97.4%), no insecticide concentrations would have been quantified (Table S3).

Overall, the small percentages of samples with quantifiable insecticide residues that we found confirm that insecticide exposure incidences occur extremely rarely in the field (i.e., less than 1% of the year, see above); consequently, the question of whether surface water exposures to

insecticide adhere to RTLs can only be addressed using insecticide concentrations $> \text{LOQ}$.

In essence, the inclusion of values below the LOQ in insecticide monitoring data evaluation underestimate the risk to aquatic life and creates a false sense of certainty and protection (4) because such an approach does not address the extremely high temporal variability of insecticide exposure in the field. In addition, the approach of assessing only peak exposure concentrations used in our meta-analysis is consistent with US EPA and EU procedures used to evaluate potential acute ecological effects (15, 45).

Distribution of insecticide measurements among surface water bodies

Overall, the 11,300 insecticide concentrations were measured in at least 1,434 discernible surface water bodies and at more than 2,500 sites. As approximately 50 studies reported multiple insecticide concentrations that were derived from several different surface waters without relating the measurements to a specific site, the exact number of investigated surface water bodies is even higher than the 1,434 water bodies specified in our dataset. However, to exclude the potential dominance of single surface water systems (i.e., a high number of concentrations measured in only one or a few surface water bodies leading to a geographical sampling bias), we analyzed our data regarding the occurrence of such spatial insecticide measurement clusters. As a result (Fig. S1), more than 50% of all surface water bodies were found to have had three or fewer insecticide measurements, and the 90th, 95th, and 99th percentiles were 19, 30, and 68 measurements per water body, respectively. Only five surface water bodies had more than 100 insecticide measurements, with a maximum of 172 concentrations per surface water body. In essence, we can exclude the possibility that insecticide concentrations derived from a few individual surface water bodies dominated our global insecticide exposure dataset.

Agricultural nonpoint source origin of insecticide concentrations

Technically speaking, the pesticide risk assessment procedures described above and the resulting RTLs are valid only for evaluating agricultural pesticide use (14, 15, 35), which is also the focus of the present meta-analysis. Although we excluded insecticide exposure data that definitely did not result from agricultural nonpoint sources, samples taken in large surface water systems might result from various sources (e.g., urban or industrial use). Therefore, we further classified water-phase concentrations into those resulting with a high certainty from agricultural nonpoint source entries (i.e., rainfall- or irrigation-induced runoff, rainfall- or irrigation-induced drainage, spray drift caused by ground-based or aerial

application, and releases from rice fields) and those that potentially, though not likely, might have resulted from other sources. This classification was based on information provided in the scientific studies; that is, we selected only those insecticide exposure concentrations (i) that the authors explicitly related to agricultural insecticide use (due to land use surrounding the sampling location, the nature of the insecticide compounds identified [e.g., some insecticides are exclusively registered for agricultural use], and the timing of sampling campaigns [e.g., dormant insecticide spraying during winter months in California]) and (ii) for which the authors provided as the definite or very likely route of entry nonpoint sources (e.g., spray drift, runoff) due to observations made during their field campaigns. These criteria enabled us to attribute specific insecticide concentrations to agricultural nonpoint source pollution with a very high degree of reliability.

If the dataset is restricted to only those insecticide concentrations definitely resulting from agricultural nonpoint source inputs (Table S4), an even higher percentage of concentrations exceed their respective RTLs. It follows that an even more stringent selection of published insecticide exposure data would highlight the failure of regulatory environmental risk assessment procedures that are employed for the agricultural use of insecticides even more strongly.

Organic carbon/water partitioning coefficient (K_{OC}) and bioavailability

The bioavailability of pesticides in surface waters generally depends on substance-specific K_{OC} values. While this parameter is less important for other insecticide classes, pyrethroid insecticides are characterized by high hydrophobicity ($K_{OC} = 10^5 - 10^7$) (46) and therefore readily bind to suspended particles, which may reduce their short-term toxicity to water column organisms (47). Analytical measurements of surface water samples without appropriate pre-filtration procedures (e.g., 0.45 μm filtration) reflect both freely dissolved and particle-associated pyrethroid concentrations. Therefore, recent scientific studies have suggested that analytical results based on such “whole water” concentrations are not directly comparable with aquatic acute toxicity effect concentrations measured in laboratory tests using water-only setups (47, 48).

However, any pre-filtering of water samples prior to analysis underestimates total pyrethroid exposure within an aquatic ecosystem due to the loss of analytes adsorbed to particles that are filtered out (45, 49), making an exposure assessment of all relevant constituents impossible. For this reason, some researchers do not recommend pre-filtering in pyrethroid surface water analysis (48, 49). Furthermore, pyrethroid adsorption is estimated to take place within several

hours (50, 51) to a few days for typical streams, which are characterized by less-than-ideal mixing conditions (51). These time spans are of toxicological concern considering that a number of studies indicated that an exposure duration of between 0.5 and 1 h to pyrethroid concentrations as low as 0.001 µg/L in the water phase can cause long-lasting, ecologically relevant effects on some aquatic organisms (52-54). In addition, ref. (55) showed that suspended particle and DOC concentrations in agriculturally influenced surface waters can be too low to have an effect on pyrethroid bioavailability reduction.

In general, the assumption that particle-sorbed pyrethroids in surface water systems are not bioavailable - or are only bioavailable to a limited extent - requires further scientific verification (48). Experimental studies demonstrating the bioavailability of hydrophobic insecticides associated with suspended sediments for bivalves (56-58) or identifying the ecotoxicological importance and bioavailability of field-relevant levels of particle-associated pyrethroids for a multispecies community typical of agricultural streams (59) indicate that toxicological effects are possible even in the presence of suspended particles. Therefore, it remains largely unclear whether and to what extent a separation between particle-free water and whole water with regard to pyrethroids is required.

To address this issue using comprehensive pyrethroid field exposure data, we screened all 919 pyrethroid water-phase measurements included in our meta-analysis for pre-filtration prior to analytical measurements. We found that 126 of the 919 pyrethroid surface water samples (13.7%) were filtered before chemical analyses, and 613 (66.7%) concentrations were reported as whole water concentration. No information regarding sample pre-treatment was available for the remaining 180 (19.6%) pyrethroid measurements in the water phase.

To analyze a potential bioavailability artifact of the strongly lipophilic pyrethroids, we performed a second linear model analysis to predict the logarithmic concentration to RTL_{SW} ratios for pyrethroids, among other variables, as a function of pre-filtration prior to analytical measurement. The following independent variables were considered again using a complete-case approach (27): log sampling interval, log catchment size, sampling date, and the dummy-coded categorical variables for country regulatory classification (HERQ countries ["0"] vs. LERQ countries ["1"]) and pyrethroid sample filtration (yes ["0"] vs. no ["1"]).

The results of the linear model analysis for pyrethroid concentrations showed that surface water samples that were filtered prior to chemical analysis led, though not significant ($p = 0.278$), to an even higher concentration to RTL_{SW} ratio compared to pyrethroids quantified in whole water samples (Table S7). This result clearly demonstrates that the comparison of RTL_{SW} exceedances for the different insecticide substance classes (i.e., significant higher

RTL_{SW} exceedances for highly sorptive pyrethroids compared to organophosphates and organochlorine insecticides) is not biased by potential pyrethroid bioavailability limitations. In consequence, RTL_{SW} exceedance frequencies were higher for pyrethroid surface water samples with pre-filtration procedures (64.5%) than for those that had not been filtered prior to the analytical determination of pyrethroid surface water concentrations (59.7%).

RTL/LOQ ratios

Statistical analysis of the different insecticide generations revealed significantly higher RTL_{SW} exceedance frequencies for pyrethroids than for organophosphates and organochlorines, with the latter two also demonstrating a significant difference (see main text, Fig. 3A, and Table S6). In fact, newer insecticide classes such as pyrethroids are characterized by a markedly higher toxicity to aquatic organisms than organophosphates, which in turn exhibit a notably higher acute toxicity in aquatic systems than organochlorines (60). The relationship between insecticide classes and increasing toxicity for aquatic organisms is also expressed in the decreasing RTL_{SW} assessed for the newer insecticide compound classes (Table S8). For example, the pyrethroid median freshwater RTL_{SW} were almost 40 times lower than the RTL_{SW} obtained for organochlorine compounds. However, median LOQs were virtually the same for organochlorines and organophosphates and were only one order of magnitude lower for pyrethroids (Table S8), such that significantly higher RTL_{SW} exceedance frequencies for pyrethroids (compared with the two older insecticide classes) could result from a methodological bias. In particular, lower distances between RTL_{SW} and LOQs of an insecticide class (e.g., pyrethroids) increase the likelihood that the concentrations exceed their RTL_{SW}.

To test the influence of this aspect, we partialled out the effects of RTL_{SW}/LOQ ratios on logarithmic concentration to RTL_{SW} ratios predicted by our main effects model (Table S6). We first regressed the dependent variable (logarithmic concentration to RTL_{SW} ratios) on logarithmic RTL_{SW}/LOQ ratios and obtained the residuals for this model. We then specified a linear model using a complete-case approach (27) that included the independent variables log sampling interval, log catchment size, sampling date, the categorical variables for country regulatory classification (HERQ countries ["0"] vs. LERQ countries ["1"]) and insecticide substance classes (organochlorines ["0"], organophosphates and carbamates ["1"], and pyrethroids ["2"]), with the residuals from the univariate regression model described above as a dependent variable.

The results of this regression analysis confirmed our findings that pyrethroid concentrations

show significantly higher RTL_{SW} exceedances than both organophosphates ($B = 0.201331$, $p < 0.001$) and organochlorines ($B = 0.296662$, $p < 0.001$), with the latter two also demonstrating a significant difference ($B = 0.095332$, $p = 0.039$) (Table S9). It follows that although the statistical consideration of the RTL_{SW}/LOQ ratios decreases the differences in predicted concentration to RTL_{SW} ratios between the insecticide classes, pyrethroids still have significantly higher RTL_{SW} exceedance frequencies compared to organophosphorus and organochlorine insecticides, with the latter two also retaining their statistically significant differences (Tables S6 and S9). In essence we conclude that despite the fact that varying RTL_{SW}/LOQ ratios have an influence on the RTL exceedance rates obtained for the different insecticide substance classes, they were not a major factor in the observed higher RTL_{SW} exceedances for newer insecticide classes.

It is worth noting that a small proportion (i.e., 6.9%) of the MICs were reported in the scientific literature based on analytical methods with LOQs that exceeded their respective RTLs. However, these cases do not contradict our findings, as all MICs detected in the field must not exceed their RTLs to avoid incidences of unacceptable effects on the freshwater biodiversity and to adhere to respective pesticide legislations. To this effect, the use of insecticide field exposure assessments with LOQs larger than the RTL should not lead to the detection of any insecticide concentration, as each individual case of RTL exceedance in the field indicates a failure of the regulatory pesticide risk assessment and a substantial risk for freshwater biodiversity, irrespective of the LOQ employed.

Interaction among substance class, country regulatory classification, and sampling date

The interaction among substance class, country regulatory classification, and sampling date derived from the linear model analysis (Table S6) contributes significantly to the variation in the concentration to RTL_{SW} ratios. To further probe this three-way interaction, we conducted simple slope tests (Table S12) and tested for significant differences for predicted logarithmic concentration to RTL_{SW} ratios for any pairs in the three-way interaction (Table S13) (cf. ref. 28). However, it is important to note here that further explanatory variables not provided in the scientific studies govern insecticide exposure in the field; the non-inclusion of these variables inevitably increases the amount of unexplained variance in our linear model analysis (Table S6).

The results of our three-way interaction analyses showed that for LERQ countries, the predicted concentration to RTL_{SW} ratios for organochlorine and organophosphorus insecticides significantly increased over time, whereas those of pyrethroids significantly

decreased (Fig. S2 and Table S12). For HERQ countries, the ratios of concentration to RTL_{SW} decreased for all three generations of insecticides; however, these declines were significant only for organophosphorus insecticides and pyrethroids. For the year 2010, the predicted concentration to RTL_{SW} ratios were significantly higher for organochlorine and organophosphorus insecticides in LERQ countries than in HERQ countries. Those for pyrethroids were also higher, but the difference was not statistically significant (see Fig. S2 and Table S13 for statistical results of predicted logarithmic concentration to RTL_{SW} ratios for pairs in this three-way interaction). In contrast, the predicted concentration to RTL_{SW} ratios for the year 1980 were higher in HERQ countries than in LERQ countries for organochlorine and organophosphorus insecticides (significant). However, no comparison between HERQ and LERQ countries could be made for this date for pyrethroids given the range of the available monitoring data (the first pyrethroid concentrations were reported in LERQ countries in the year 1993) for this compound class (see, also, Fig. S2, C and D).

The development and application of legislative and regulatory prescriptions for pesticide use in HERQ countries in recent decades (Table S2) may help to explain the decreasing risks arising from agricultural insecticide applications in those countries over time. In contrast, pesticide use in LERQ countries has increased rapidly in recent decades, but because of prioritizing food production maximization over environmental considerations, these countries only weakly regulate pesticide use and application (61-63). As a result, increasing organochlorine and organophosphorus insecticide concentrations and overall threshold level exceedance rates in surface waters can be observed in these countries. In addition to LERQ countries' weak regulatory frameworks and rule enforcement, farmers' limited knowledge of appropriate pesticide use and environmental awareness also contribute to higher exposure and therefore risks for surface water systems (61, 63). However, in contrast to those for organochlorine and organophosphorus insecticides, pyrethroids' predicted concentration to RTL_{SW} ratios showed a significant decrease in LERQ countries during the last two decades (Fig. S2, A to D, and Table S12). Although the reasons for this decrease are not completely clear, Fig. S2D indicates that only four studies with 27 concentrations (i.e., only 2.9% of all [n = 919] pyrethroid surface water concentrations documented in the scientific literature), which all stemmed from Asia, were available for the period 2005–2011. It follows that the predicted decrease of concentration to RTL_{SW} ratios for the years 1995 to 2010 could be an information bias resulting from a lack of different field investigations on pyrethroid surface water concentrations in LERQ countries, which, however, is not the case for the predicted high concentration to RTL_{SW} ratios for 1995, as ten field studies with 99 concentrations from

Africa, Asia, Europe, and South America were available for the time span 1999–2004 (Fig. S2, *C* and *D*). Overall, the data availability on pyrethroid surface water exposure in LERQ countries must be judged as too weak to definitively conclude that their environmental risk for aquatic ecosystems decreased considerably between 1995 and 2010. It follows that more field investigations are needed to clarify the actual environmental risks of agricultural pyrethroid use in LERQ countries worldwide.

Regarding differences among specific insecticide classes, pyrethroids showed a significantly higher predicted risk for surface waters systems than the other two classes in HERQ countries for 1995 and 2010 (Table S13 and Fig. S2, *A* to *C*). Although the predicted concentration to RTL_{SW} ratios were slightly higher for organophosphorus insecticides for the year 1980, the difference with respect to pyrethroids was not statistically significant, and both were significantly higher than those of organochlorine insecticides. Pyrethroids' predicted risks for aquatic ecosystems were also significantly higher than those for organochlorine and organophosphorus insecticides in LERQ countries for the year 1995. However, no statistically significant difference between concentration to RTL_{SW} ratios of organochlorines and pyrethroids derived from LERQ country data could be observed for 2010, and organophosphorus insecticides exceeded the other two insecticide classes significantly. Organophosphorus insecticide risks for surface waters were predicted to be significantly higher in HERQ countries than those arising from organochlorine insecticides for 1980 and 1995 as well as for 1995 and 2010 when considering LERQ countries (Fig. S2, *A* to *C*, and Table S13).

Overall, the evaluation of real-world monitoring data as presented here does not confirm the assumption that prevails in the scientific literature (64-68) that newer insecticide classes are more environmental friendly than older ones, at least when short-term acute risks for aquatic ecosystems are considered. The probable reason for this observation is the increasing invertebrate toxicity that has accompanied the development of newer insecticide classes in recent decades (60) and that often triggers RTL_{SW} settings for insecticides. In addition, ref. 41 found that the EU regulatory exposure assessment via FOCUS models is significantly less protective in predicting pyrethroid field concentrations than organochlorine and organophosphorus concentrations. This finding may also be true for regulatory pesticide model-based exposure assessments in other countries.

SI Figures

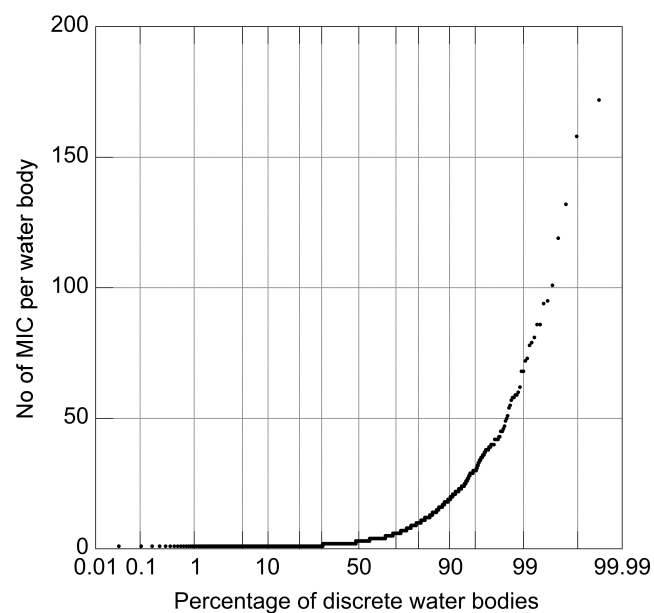


Fig. S1. Number of measured insecticide concentrations (MICs, $n = 11,300$) reported for individual surface water bodies ($n = 1,434$). Please note that the actual number of discernible water bodies is higher than 1,434 because approximately 50 studies did not specify the exact location of sites with MICs and multiple water bodies were analyzed for insecticide exposure.

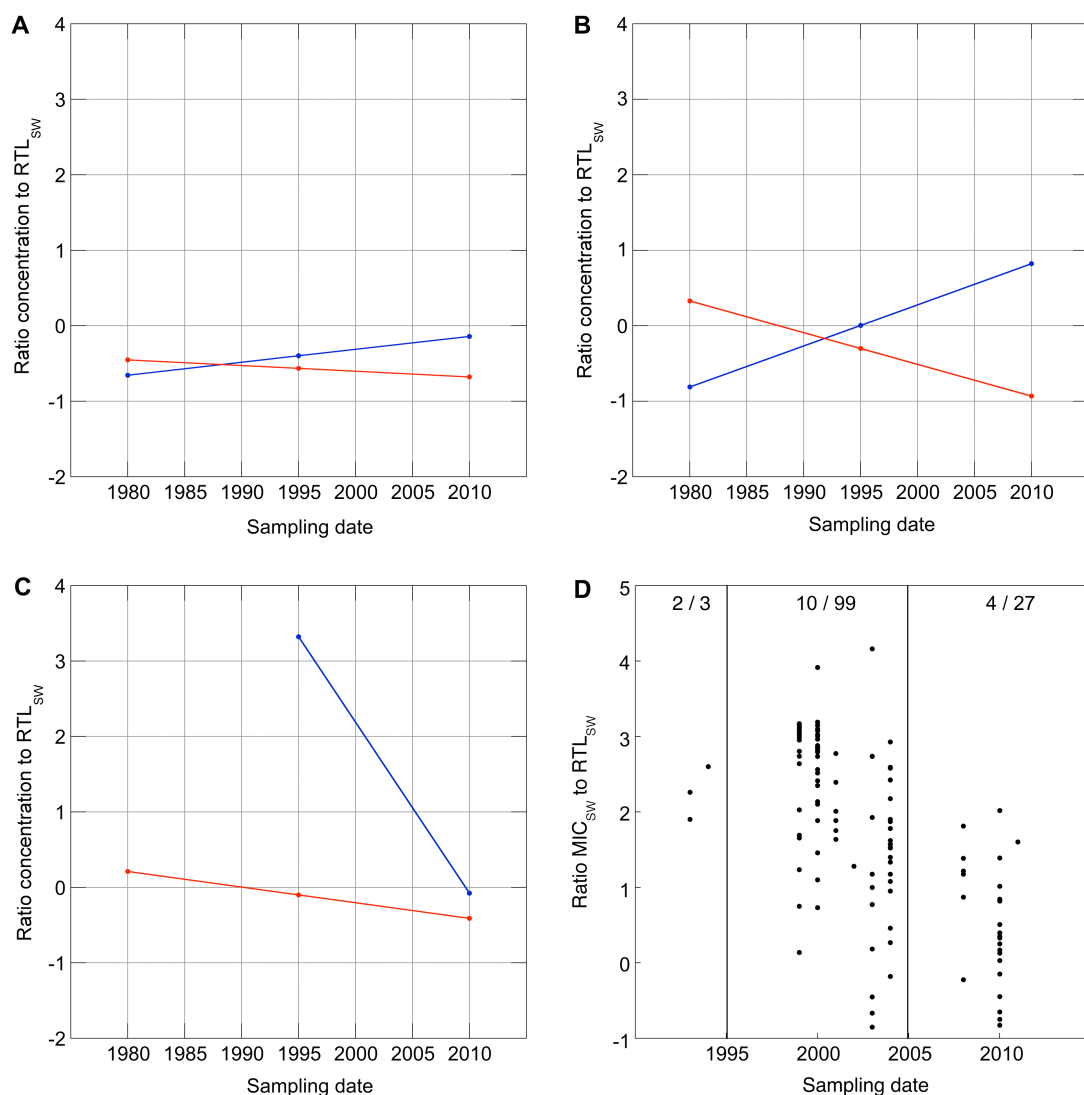


Fig. S2. Three-way interaction among insecticide substance class ([A] organochlorine insecticides; [B] organophosphate insecticides; [C] pyrethroids), country regulatory classification (blue lines: LERQ countries; red lines: HERQ countries), and sampling date versus predicted logarithmic water-phase concentration to regulatory threshold level (RTL_{SW}) ratios. Please note that no predicted concentration to RTL_{SW} ratios were calculated for pyrethroids in LERQ countries for the year 1980 (C) because no field study data were available before 1993 (see, also, Table S13). (D) Temporal evolution of logarithmic measured aqueous insecticide concentration (MIC_{SW}) to RTL_{SW} ratios ($n = 129$) derived for pyrethroids from field studies conducted in LERQ countries. Only pyrethroid concentrations available for the linear model analysis are shown. The first figures indicate the numbers of field studies, and the second figures indicate the numbers of concentrations available for specific time periods.

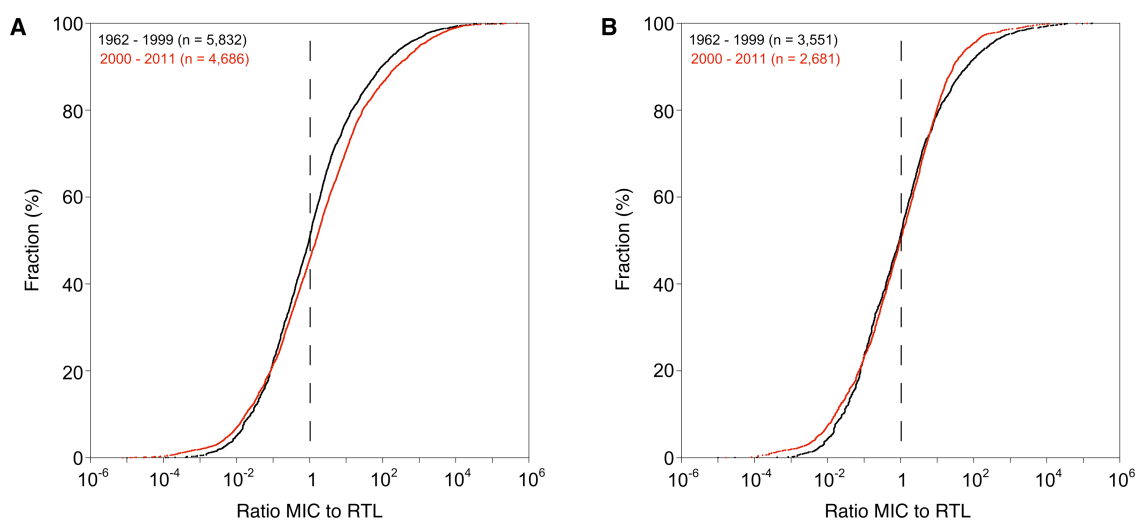


Fig. S3. Distribution curves for reported measured insecticide concentrations (MICs) in water and sediment relative to the respective regulatory threshold levels (RTLs) separated according to whether the values were measured before (i.e., 1962 – 1999; black dots) or after (i.e., 2000 – 2011; red dots) the year 2000. (A) Insecticide exposure data for global surface waters; 5,832 concentrations were measured before and 4,686 concentrations were measured after the year 2000. (B) Insecticide exposure data for highly regulated countries (Table S10) only; 3,551 concentrations were measured before and 2,681 concentrations were measured after the year 2000.

SI Tables

Table S1. Insecticides included in the meta-analysis and their corresponding regulatory threshold levels for water (RTL_{SW}) and sediments (RTL_{SED}). See *SI Methods* for further details on RTL_{SW} and RTL_{SED} derivation. n.s.: not specified (tau-fluvalinate [three concentrations found in sediments] has no RTL_{SED} or MPC [no maximum permissible concentration or toxicity endpoint available]. Therefore, of the total reported 11,300 concentrations, only 11,297 concentrations were available for all comparisons with threshold levels). - indicates that no freshwater (FW), estuarine water (EST), or sediment concentrations were reported for this insecticide in the literature; sediment refers to sediment and suspended particle concentrations. No US EPA risk assessment documents were available for fenvalerate; thus, toxicity data from the OPP Pesticide Ecotoxicity Database (13) were used for FW and EST RTL_{SW} derivation. MPCs (referred to as RTL_{SED}) for cyfluthrin, esfenvalerate, fenpropathrin, and fenvalerate were derived based on ecotoxicological endpoints published in the scientific literature by applying the modified EPA method according to ref. 19 and ref. 22. Insecticide classes are abbreviated as follows: organochlorine (OC), organophosphate (OP), carbamate (Carb), pyrethroid (Pyr), and neonicotinoid (Neo).

Insecticide	Class	RTL _{SW} (µg/L)			RTL _{SED} (µg/kg)
		North America FW/EST	Europe	Worldwide FW/EST	
Endosulfan	OC	0.05 ⁽⁶⁹⁾ /0.02 ⁽⁶⁹⁾	1.3 ⁽¹⁸⁾	0.675/0.66	0.026 ⁽¹⁹⁾
Azinphos-methyl	OP	0.08 ⁽⁷⁰⁾ /0.105 ⁽⁷⁰⁾	0.32 ⁽⁷¹⁾	0.2/0.2125	0.89 ⁽¹⁹⁾
Chlorpyrifos	OP	0.05 ⁽⁷²⁾ /0.0175 ⁽⁷²⁾	0.1 ⁽⁷³⁾	0.075/0.05875	1.1 ⁽¹⁹⁾
Diazinon	OP	0.105 ⁽⁷⁴⁾ /2.1 ⁽⁷⁵⁾	2.4 ⁽⁷⁶⁾	1.2525/2.25	0.95 ⁽¹⁹⁾
Malathion	OP	0.005 ⁽⁷⁷⁾ /0.005 ^(77,78)	1.25 ⁽⁷⁹⁾	0.6275/0.6275	0.9 ⁽¹⁹⁾
Parathion-ethyl	OP	0.02 ⁽⁸⁰⁾ /0.0535 ⁽⁸⁰⁾	0.024 ⁽⁸¹⁾	0.022/0.03875	0.13 ⁽¹⁹⁾
Parathion-methyl	OP	0.485 ⁽⁸²⁾ /0.175 ⁽⁸³⁾	0.073 ⁽⁸⁴⁾	0.279/0.124	0.96 ⁽¹⁹⁾
Carbofuran	Carb	1.115 ⁽⁸⁵⁾ /2.3 ⁽⁸⁵⁾	0.0205 ⁽⁸⁶⁾	0.56775/1.16025	0.22 ⁽⁸⁶⁾
Acrinathrin	Pyr	-/-	0.0087 ⁽⁸⁷⁾	-/-	-
Bifenthrin	Pyr	0.075 ⁽⁸⁸⁾ /0.002 ⁽⁸⁸⁾	0.005 ⁽⁸⁹⁾	0.04/0.0035	4 ⁽⁸⁹⁾
Cyfluthrin	Pyr	0.0125 ⁽⁹⁰⁾ /0.0012 ⁽⁹⁰⁾	0.0068 ^(91,92)	0.00965/0.004	0.137 ⁽⁹³⁾
β-cyfluthrin	Pyr	-/-	0.00068 ⁽⁹⁴⁾	-/-	-
Cypermethrin	Pyr	0.0018 ⁽⁹⁵⁾ /-	0.025 ⁽⁹⁶⁾	0.0134/-	1.8 ⁽⁹⁵⁾
α-cypermethrin	Pyr	0.0018 ⁽⁹⁵⁾ /-	0.015 ⁽⁹⁷⁾	0.0084/-	1.8 ⁽⁹⁵⁾
ζ-cypermethrin	Pyr	0.0018 ⁽⁹⁵⁾ /-	-	-/-	-
Deltamethrin	Pyr	0.055 ⁽⁹⁸⁾ /0.00085 ⁽⁹⁸⁾	0.0032 ⁽⁹⁹⁾	0.0291/0.002025	1.3 ⁽¹⁹⁾
Esfenvalerate	Pyr	0.025 ⁽¹⁰⁰⁾ /0.025 ^(100,101)	0.01 ⁽¹⁰²⁾	0.0175/0.0175	0.41738 ⁽⁹³⁾
Fenpropathrin	Pyr	0.265 ⁽¹⁰³⁾ /0.0105 ⁽¹⁰³⁾	0.0053 ⁽¹⁸⁾	0.13515/0.0079	0.645 ⁽¹⁰⁴⁾
Fenvalerate	Pyr	0.016 ⁽¹⁰⁵⁾ /0.004 ⁽¹⁰⁶⁾	0.0022 ⁽¹⁸⁾	0.0091/0.0031	0.88 ⁽¹⁰⁷⁾
λ-cyhalothrin	Pyr	0.0035 ⁽¹⁰⁸⁾ /0.00205 ⁽¹⁰⁸⁾	0.0021 ⁽¹⁰⁹⁾	0.0028/0.002075	10.5 ⁽¹⁰⁹⁾
Permethrin	Pyr	0.0106 ⁽¹¹⁰⁾ /0.009 ⁽¹¹⁰⁾	0.025 ⁽¹⁸⁾	0.0178/0.017	0.87 ⁽¹⁹⁾
Tau-fluvalinate	Pyr	0.175 ⁽¹¹¹⁾ /-	0.022 ⁽¹¹²⁾	0.0985/-	n.s.
Tefluthrin	Pyr	-/-	-	-/-	47 ⁽¹¹³⁾

Tralomethrin	Pyr	0.0195 ⁽¹¹⁴⁾ /-	-	-/-	-
Acetamiprid	Neo	10.5 ⁽¹¹⁵⁾ /-	0.5 ^(116, 117)	5.5	-
Imidacloprid	Neo	34.5 ⁽¹¹⁸⁾ /-	0.3 ⁽¹¹⁹⁾	17.4/-	-
Thiacloprid	Neo	-/-	1.57 ⁽¹²⁰⁾	-/-	-
Thiamethoxam	Neo	-/-	2.8 ⁽¹²¹⁾	-/-	-

Table S2. List of major international pesticide regulations and guidelines enforced since 1988 in chronological order.

Regulation / guideline
FIFRA Amendments US Federal Law
91/414/EEC EU Pesticide Directive
EPA Risk Assessment “New Paradigm”
EWOFFT (European Workshop on Freshwater Field Test) mesocosm guidance
EPA/ACPA ARAMDG (Aquatic Risk Assessment Mitigation Dialog Group)
Sediment toxicity testing (SETAC guidance document)
“Ganzelmeier/Rautmann” basic spray drift values
FQPA (Food Quality Protection Act)
ECCO (European Community Co-Ordination) aquatic terrestrial guidance
EPA “safer pesticide” program
OPPTS (Office of Prevention, Pesticides and Toxic Substances) study guideline revisions
EMWAT (Endocrine Modulators and Wildlife: Assessment and Testing guideline; EPA, OECD)
ESCORT I (European Standard Characteristics of non-target Arthropod Regulatory Testing) guideline
HARAP (Higher Tier Aquatic Risk Assessment for Pesticides) SETAC guidance document
FOCUS (FORum for the Coordination of pesticide fate models and their USE) aquatic exposure assessment
ECOFRAM (Ecological Committee on FIFRA Risk Assessment Methods)
CLASSIC (Community Level Aquatic System Studies Interpretation Criteria) SETAC guidance document
ESCORT II (European Standard Characteristics of non-target arthropod Regulatory Testing) guideline
EU DG SANCO Guidance document on Aquatic ecotoxicology revision 4
EUPRA (Probabilistic Risk Assessment for the environmental impact of plant protection products)
EPPO (European and Mediterranean Plant Protection Organisation) guideline revisions
EPA non-target plant Scientific Advisory Panel
1999/45/EEC EU Classification & Labeling Directive
2000/60/EEC EU Water Framework Directive
EU Water Framework Directive amendment priority pollutants
2002/17 EEC EU Environmental Liability Directive
EU Thematic Strategy on Sustainable Use (COM(02)349)
Stockholm Convention on Persistent Organic Pollutants
Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade
EPFES (Effects of Plant Protection Products on Functional Endpoints in Soil) guidance document
FOCUS Working Group on Landscape and Mitigation Factors in Ecological Risk Assessment
ELINK (Linking Aquatic Exposure and Effects in the Registration Procedure of plant protection products)
EU Directive 2009/128/EC Sustainable Use of Pesticides
OECD Strategic Approach in Pesticide Risk Reduction (ENV/JM/MONO(2009)38)
Regulation (EC) 1107/2009 EU Pesticide Directive revision
EFSA Guidance document on tiered risk assessment for plant protection products for aquatic organisms

Table S3. Descriptive statistics (number of concentration measurements) regarding important parameters related to the global insecticide exposure dataset and information on the relation of measured (i.e., quantified) insecticide concentrations (MICs) to the estimated population of analyses conducted.

Parameter^a (number of MICs with information)	Minimum	25th percentile	Median	75th percentile	Maximum
MICs per country ^b (n = 11,300)	1	4	31	111	3,854
Sampling date (year; n = 10,521)	1960	1993	1999	2004	2011
Catchment size (km ² ; n = 9,290)	0.002	10	200	2,750	3,400,000
Sampling interval (days; n = 8,427)	0.0416 ^c	2	15	30	180
Hydrology (n = 10,715)	Lotic surface waters: 8,357 (78%); lentic surface waters: 2,358 (22%)				
Surface water classification (n = 11,300)	Freshwater systems: 9,910 (87.7%); estuarine waters: 1,390 (12.3%)				
Route of entry (n = 11,300)	Nonpoint source ^d : 7,371 (65.2%); runoff: 2,846 (25.2%); rice field effluent: 431 (3.8%); spray drift: 346 (3.1%); aerial application: 179 (1.6%); drainage: 127 (1.1%)				
Relation of MICs to the population of analytical measurements ^e	Total analyses conducted ^e : 434,615 (100%) MIC < LOQ ^f : 423,315 (97.4%) MIC > LOQ ^f : 11,300 (2.6%) MIC > LOQ ^f & RTL ^g : 5,915 (1.4%; 52.4% of cases with MIC > LOQ)				

a: Smaller numbers for some parameters are due to missing information in the studies.

b: Data are available for 73 countries; see Table S10 for details.

c: Event sampling

d: Nonpoint source indicates that the exact route of entry was not further specified in the publications

e: Estimated using information from 11 detailed scientific monitoring studies (see *SI Discussion* "Evaluation of insecticide monitoring data")

f: Limit of quantification

g: Regulatory threshold level

Table S4. Classification of measured insecticide water-phase concentrations (MIC_{SW} ; $n = 8,166$) related to regulatory threshold levels (RTL_{SW}), considering the certainty regarding agricultural nonpoint sources as the origin of exposure.

Classification^a	No. of MIC_{SW} values less than RTL_{SW} (%)	No. of MIC_{SW} values exceeding RTL_{SW} (%)
Definitive agricultural nonpoint source origin ($n = 2,554$) (31.3%)	1,285 (50.3)	1,269 (49.7)
No definitive agricultural nonpoint source origin ^b ($n = 5,612$) (68.7%)	3,550 (63.3)	2,062 (36.7)

a: In addition to information on the route of entry and the origin of the MIC_{SW} provided in the studies, the classification used was based on the surrounding land use of the sampling locations, the insecticide compounds identified (e.g., some are exclusively registered for agricultural use), and the timing of the sampling campaigns (e.g., dormant insecticide spraying during the winter months in California).

b: The classification “No definitive agricultural nonpoint source origin” does not mean that MIC_{SW} originated from non-agricultural or point sources because this classification was often applied because limited information was provided in the studies.

Table S5. Market introduction (23, 122), development of insecticide market shares (123), and mode of action (8) for major insecticide classes.

Insecticide class	Introduction to the market	Insecticide market share (%) 1990 / 2008	Mode of action
Organochlorines	1940	- / -	GABA-gated chloride channel antagonists
Organophosphates/Carbamates ^a	1950/1962	59 / 24.4	Acetylcholinesterase inhibitors
Pyrethroids	1973	18 / 15.5	Sodium channel modulators
Neonicotinoids	1991	0 / 23.7	Nicotinic acetylcholine receptor agonists

a: Named “organophosphates” in the main text.

Table S6. The results of linear model analyses (main effects model and full model including two- and three-way interactions) for predicting logarithmic insecticide water-phase concentration to RTL_{SW} ratios ($n = 5,746$). Substance class (SC) (reference category: organochlorine insecticides) and country regulatory classification (CRC) (reference category: high environmental regulatory quality) were entered as dummy-coded variables, and catchment size and sampling interval were entered as log-transformed variables. The same main effects analysis was also carried out using the insecticide substance class organophosphates/carbamates as the reference category to calculate the significance level of pyrethroids vs. organophosphates/carbamates ($B = 0.435925$; t -value = 8.170 ; $p < 0.001$). The insecticide substance class neonicotinoid was excluded due to the small number of cases ($n = 72$) available for analysis.

Step	Multiple R ²	Predictors within final models	Estimate	t-value
Main effects model	0.2331	Intercept	28.3543***	7.159
		Catchment size	-0.2049***	-19.355
		Sampling interval	-0.3669***	-24.701
		Sampling date	-0.014***	-7.166
		SC (OP) ^a	0.4327***	10.870
		SC (Pyr) ^a	0.8687***	14.590
		CRC (LERQ) ^a	0.6349***	17.899
Model with two-way and three-way interactions^b	0.312 (ΔR^2 : 0.0789***)	Intercept	15.22	1.373
		Catchment size	-0.2189***	-21.390
		Sampling interval	-0.3594***	-25.354
		Sampling date	-0.0075	-1.353
		SC (OP) ^a	69.19***	5.608
		SC (Pyr) ^a	26.84	1.668
		CRC (LERQ) ^a	-48.95**	-2.738
		Sampling date x CRC (LERQ) ^a	0.02462**	2.749
		SC (OP) ^a x CRC (LERQ) ^a	-143.2***	-7.009
		SC (Pyr) ^a x CRC (LERQ) ^a	462.9***	8.936
		Sampling date x SC (OP) ^a	-0.03455***	-5.584
		Sampling date x SC (Pyr) ^a	-0.01322	-1.641
		Sampling date x SC (OP) ^a x CRC (LERQ) ^a	0.07185***	7.024
		Sampling date x SC (Pyr) ^a x CRC (LERQ) ^a	-0.2304***	-8.902

a: OP: organophosphates/carbamates; Pyr: pyrethroids; LERQ: low environmental regulatory quality countries

b: See, also, Fig. S2 for a graphical presentation of the three-way interaction.

Significance codes: *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$

Table S7. The results of linear model analyses for predicting logarithmic concentration to RTL_{SW} ratios ($n = 650$) for pyrethroid surface water concentrations as a function of sample filtration. Country regulatory classification (reference category: high environmental regulatory quality) and pyrethroid sample filtration (reference category: yes) were entered as dummy-coded variables, and catchment size and sampling interval were entered as log-transformed variables.

	Estimate	t-value	p-value
Intercept	101.329221	8.390	<0.001
Catchment size	-0.180251	-5.095	<0.001
Sampling interval	-0.261243	-9.290	<0.001
Sampling date	-0.050284	-8.342	<0.001
CRC (LERQ) ^a	0.997281	6.473	<0.001
Pyrethroid sample filtration ^b (no)	-0.147252	-1.086	0.278

a: Low environmental regulatory quality countries

Multiple R^2 : 0.3012; adjusted R^2 : 0.2958

Table S8. Central tendencies (mean and median) of organochlorines ($n = 515$), organophosphates ($n = 1,762$), and pyrethroids ($n = 546$) limit of quantification (LOQ) (derived from studies reporting respective measured insecticide concentrations), mean, and median of freshwater (FW) regulatory threshold levels (RTL_{SW}) (expressed as the average of European and North American FW RTL_{SW} , as listed in Table S1) of the different insecticide classes and the mean and median of specific RTL_{SW}/LOQ ratios for each insecticide concentration.

	Organochlorines	Organophosphates	Pyrethroids
LOQ ($\mu\text{g/L}$) (mean / median)	0.045 / 0.01	0.039 / 0.01	0.041 / 0.001
FW RTL_{SW} ($\mu\text{g/L}$) (mean / median)	0.675 / 0.675	0.432 / 0.279	0.035 / 0.0175
RTL_{SW}/LOQ -ratio (mean / median)	658.1 / 45.5	952.5 / 12.5	36.4 / 6.3

Table S9. The results of linear model analyses ($n = 2,367$) for predicting the residuals of the linear model “log concentration to RTL_{SW} ratio = $0.83789 - 0.87558 \times \log RTL_{SW}/LOQ$ -ratio”. Substance class (reference category: organochlorine insecticides) and country regulatory classification (reference category: high environmental regulatory quality) were entered as dummy-coded variables, and catchment size and sampling interval were entered as log-transformed variables. The same regression model was also analyzed using the insecticide substance class organophosphates/carbamates as the reference category to calculate the significance level of pyrethroids vs. organophosphates/carbamates ($B = 0.201331$; t -value = 5.101; $p < 0.001$).

	Estimate	t-value	p-value
Intercept	15.518538	3.946	<0.001
Catchment size	-0.050470	-5.307	<0.001
Sampling interval	-0.129792	-10.359	<0.001
Sampling date	-0.007756	-3.934	<0.001
Substance class (OP) ^a	0.095332	2.069	0.0386
Substance class (Pyr) ^a	0.296662	5.168	<0.001
CRC (LERQ) ^a	0.137455	3.673	<0.001

a: OP: organophosphates/carbamates; Pyr: pyrethroids; LERQ: low environmental regulatory quality countries
Multiple R^2 : 0.07274; adjusted R^2 : 0.07038

Table S10. Classification of countries (n = 73) according to their environmental regulatory quality and number of measured insecticide concentrations (MICs) per country. See *SI Methods* for the detailed classification procedure. HERQ: High Environmental Regulatory Quality, LERQ: Low Environmental Regulatory Quality; ERRI: Environmental Regulatory Regime Index (24); RQ percentile rank: Regulatory Quality percentile rank (25), subdivided as follows: I: Regulatory Quality Percentile Rank 0-25; II: Regulatory Quality Percentile Rank 25-50; III: Regulatory Quality Percentile Rank 50-75; IV: Regulatory Quality Percentile Rank 75-100. GNI per capita: Gross National Income (GNI) per capita (26) classified as follows: 1: Low-income economies GNI per capita: \$1,025 or less; 2: Lower-middle-income economies GNI per capita: \$1,026-\$4,035; 3: Upper-middle-income economies GNI per capita: \$4,036-\$12,475; 4: High-income economies GNI per capita: \$12,476 or more. n.s.: not specified.

Country classification ^a		Classification category		
HERQ	LERQ	ERRI score	RQ percentile rank	GNI per capita
Australia (531)		pos. (> 1)	IV	4
Belgium (26)		pos. (> 1)	IV	4
Bahrain (4)		n.s.	IV	4
Canada (632)		pos. (> 1)	IV	4
Cyprus (3)		n.s.	IV	4
Denmark (7)		pos. (> 1)	IV	4
France (46)		pos. (> 1)	IV	4
Germany (138)		pos. (> 1)	IV	4
Hungary (3)		pos. (< 1)	IV	4
Israel (1)		pos. (< 1)	IV	4
Italy (152)		pos. (< 1)	IV	4
Japan (477)		pos. (> 1)	IV	4
Netherlands (60)		pos. (> 1)	IV	4
Norway (3)		pos. (> 1)	IV	4
Poland (33)		pos. (< 1)	IV	4
Singapore (6)		pos. (> 1)	IV	4
Spain (415)		pos. (< 1)	IV	4
Sweden (17)		pos. (> 1)	IV	4
Switzerland (6)		pos. (> 1)	IV	4
Taiwan (41)		n.s.	IV	4
United Kingdom (79)		pos. (> 1)	IV	4
United States (3854)		pos. (> 1)	IV	4
	Albania (5)	n.s.	III	2
	Argentina (258)	neg.	II	3
	Bangladesh (20)	neg.	I	1
	Belize (2)	n.s.	II	2
	Benin (13)	n.s.	II	1
	Brazil (192)	neg.	III	3
	Bulgaria (1)	neg.	III	3

Country classification ^a		Classification category		
HERQ	LERQ	ERRI score	RQ percentile rank	GNI per capita
	Chile (29)	pos. (< 1)	IV	3
	China (411)	neg.	II	3
	Costa Rica (45)	neg.	III	3
	Cote d'Ivoire (12)	n.s.	I	2
	Egypt (111)	neg.	II	2
	El Salvador (2)	neg.	III	2
	Fiji Islands (1)	n.s.	II	2
	Gambia (4)	n.s.	II	1
	Ghana (51)	n.s.	III	2
	Greece (487)	neg.	III	4
	Honduras (17)	neg.	II	2
	India (551)	neg.	II	2
	Indonesia (60)	neg.	II	2
	Iran (368)	n.s.	I	3
	Jamaica (410)	neg.	III	3
	Jordan (2)	pos. (< 1)	III	3
	Kenya (164)	n.s.	II	1
	Korea (10)	neg.	IV	4
	Macedonia (12)	n.s.	III	3
	Malaysia (57)	neg.	III	3
	Mexico (251)	neg.	III	3
	Moldova (4)	n.s.	III	2
	Nicaragua (70)	neg.	II	2
	Nigeria (69)	neg.	II	2
	Oman (4)	n.s.	III	4
	Pakistan (31)	n.s.	II	2
	Panama (1)	neg.	III	3
	Philippines (101)	neg.	II	2
	Portugal (94)	neg.	III	4
	Qatar (3)	n.s.	III	4
	Romania (5)	neg.	IV	3
	Serbia (1)	n.s.	III	3
	South Africa (360)	neg.	III	3
	Sri Lanka (37)	neg.	III	2
	Tanzania (12)	n.s.	II	1
	Thailand (69)	neg.	III	3
	Togo (4)	n.s.	I	1
	Tunisia (4)	n.s.	II	3
	Turkey (250)	n.s.	III	3

Country classification^a		Classification category		
HERQ	LERQ	ERRI score	RQ percentile rank	GNI per capita
	Uganda (18)	n.s.	III	1
	United Arab Emirates (2)	n.s.	III	4
	Venezuela (41)	neg.	I	3
	Vietnam (35)	neg.	II	2
	Zambia (5)	n.s.	II	2

a: Numbers in brackets denote MICs per country.

Table S11. Descriptive statistics for potential covariates of aqueous-phase measured insecticide concentrations (MIC_{SW}) separated by countries' environmental regulatory quality. Note that the cumulative statistical sample sizes for watershed catchment sizes ($n = 6,780$), sampling intervals ($n = 6,445$), and sampling dates ($n = 7,633$) are smaller than the total number of MIC_{SW} present in surface water ($n = 8,166$) due to missing data in the studies evaluated. HERQ: High Environmental Regulatory Quality, LERQ: Low Environmental Regulatory Quality; see Table S10 for the classification of countries according to their environmental regulatory quality.

Covariate	Mean	Median	Range
Catchment size			
HERQ ($n = 4,341$)	9,998 km ²	152.5 km ²	0.002 – 2,900,000 km ²
LERQ ($n = 2,439$)	60,213 km ²	400 km ²	0.1 – 3,400,000 km ²
Sampling Interval			
HERQ ($n = 4,167$)	25.4 d	10 d	Event – 180 d
LERQ ($n = 2,278$)	44.8 d	30 d	Event – 180 d
Sampling date			
HERQ ($n = 4,775$)	-	1997	1960 – 2011
LERQ ($n = 2,858$)	-	1999	1970 – 2011

Table S12. Test of simple slopes (28) for the three-way interaction of country regulatory classification x substance class x sampling date (see, also, Fig. S2) specified using the full model for predicting logarithmic concentration to RTL_{SW} ratios (see Table S6). Substance classes (SC) are abbreviated as follows: organochlorine (OC), organophosphate (OP), pyrethroid (Pyr). Country regulatory classifications (CRC) are abbreviated as follows: HERQ (high environmental regulatory quality), LERQ (low environmental regulatory quality).

SC / CRC	Simple slope	t-value	p-value
OC / HERQ	-0.007521	-1.353	0.17625
OC / LERQ	0.0171	2.43	0.01512
OP / HERQ	-0.04207	-15.711	< 0.001
OP / LERQ	0.0544	12.991	< 0.001
Pyr / HERQ	-0.02074	-3.538	< 0.001
Pyr / LERQ	-0.22649	-9.622	< 0.001

Table S13. The results of the modified Johnson–Neyman technique (28) to test for significant differences for predicted logarithmic concentration to RTL_{SW} ratios for any pairs of the three-way interaction country regulatory classification x substance class x sampling date (see, also, Fig. S2). Substance classes are abbreviated as follows: organochlorine (OC), organophosphate (OP), pyrethroid (Pyr). Country regulatory classifications are abbreviated as follows: HERQ (high environmental regulatory quality), LERQ (low environmental regulatory quality).

Pair tested for significant difference (first item denotes the reference category)	Estimate	t-value	p-value
HERQ vs LERQ: 1980, OC	-0.207742	-1.277	0.20148
HERQ vs LERQ: 1980, OP	-1.105435	-11.465	<0.001
HERQ vs LERQ: 1980, Pyr	n/a ^a	n/a ^a	n/a ^a
HERQ vs LERQ: 1995, OC	0.161536	2.322	0.020274
HERQ vs LERQ: 1995, OP	0.341623	7.952	<0.001
HERQ vs LERQ: 1995, Pyr	3.476451	16.358	<0.001
HERQ vs LERQ: 2010, OC	0.530814	3.818	<0.001
HERQ vs LERQ: 2010, OP	1.788681	24.325	<0.001
HERQ vs LERQ: 2010, Pyr	0.390167	1.858	0.063156
OC vs OP: 1980, HERQ	0.780945	7.675	<0.001
OC vs Pyr: 1980, HERQ	0.665452	4.073	<0.001
OP vs Pyr: 1980, HERQ	-0.115493	-0.797	0.425671
OC vs OP: 1980, LERQ	-0.116748	-0.734	0.4627
OC vs Pyr: 1980, LERQ	n/a ^a	n/a ^a	n/a ^a
OP vs Pyr: 1980, LERQ	n/a ^a	n/a ^a	n/a ^a
OC vs OP: 1995, HERQ	0.262673	4.973	<0.001
OC vs Pyr: 1995, HERQ	0.467186	5.87	<0.001
OP vs Pyr: 1995, HERQ	0.204513	3.15	0.001639
OC vs OP: 1995, LERQ	0.442760	7.275	<0.001
OC vs Pyr: 1995, LERQ	3.782101	18.064	<0.001
OP vs Pyr: 1995, LERQ	3.339341	16.133	<0.001
OC vs OP: 2010, HERQ	-0.2556	-2.291	0.022025
OC vs Pyr: 2010, HERQ	0.268921	2.185	0.028955
OP vs Pyr: 2010, HERQ	0.52452	6.62	<0.001
OC vs OP: 2010, LERQ	1.002267	8.997	<0.001
OC vs Pyr: 2010, LERQ	0.128273	0.221507	0.562548
OP vs Pyr: 2010, LERQ	-0.873994	-4.196	<0.001

a: Data not available due to a lack of field study data for pyrethroids in LERQ countries before 1993 (see, also, Fig. S2).

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